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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,238	HALE ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 29-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-28 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application Election/Restrictions

Applicant's election with traverse of Group VI (claims 21-28 and 49) in the reply filed on October 9, 2006 is acknowledged. The traversal is on the ground(s) that at least Groups I, V-IX, and XI are linked so as to form a single general inventive concept because Groups I, V-IX and XI have a common special technical feature that defines a contribution over the prior art. Applicant argues that a search for any Group from Groups I, V-IX and XI would uncover the references for Groups I, V-IX and XI. Applicant argues that the pending claims of at least Groups I, IV- IX, and XI have in common a special technical feature. Applicant argues that the complex comprising sambiasin-1, presenilin-1 and nicastrin is novel. Applicant's arguments have been fully considered but they are not found persuasive because sambiasin-1 is known in the art and the complex of presenilin and nicastrin is also known in the art as stated in the previous office. Therefore, claim 1 has no special technical feature that defines a contribution over the prior art. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. In addition, each group of Groups I, V-IX and XI has its different technical feature, which requires different search and analyses. The requirement is still deemed proper and is therefore made FINAL.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The disclosure is objected to because of the following informalities: the degree sign of 65°C described on p.28, last line is missing. Appropriate correction is required.

Claim Objections

Claims 21-28 and 49 are objected to because the claims recite claim 1 and claim 9, which are non-elected claims. Claims 21 and 22 depend from claim 1. Claim 49 depends from claim 9. Claims 23-28 depend from claim 22. However, claims 1 and 9 are non-elected claims. Applicant is required to amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21-28 and 49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" use for the claimed invention. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966):

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

The instant application has provided a description of a method for screening for a molecule that modules the function, activity, composition of a protein complex having a first protein sambiasin-1 (SEQ ID NO:1) and a second protein selected from presenilin-1 (SEQ ID NO:2) and/or nicastrin (SEQ ID NO:3). The specification describes identifying a protein complex comprising sambiasin-1 (SEQ ID NO:1) and presenilin-1 (SEQ ID NO:2) by immunoprecitating mouse brain homogenates with anti-presenilin-1 antibody and analyzing the content of the protein by mass spec. However, the instant application fails to disclose a specific biological significance of the disclosed complex or its relevance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect. Based on the description, the protein complex might be associated with processes related to Alzheimer's disease or embryo development or developmental disorders because presenilin-1 and nicastrin are involved in amyloid precursor protein (APP) processing and Notch cleavage based on

the prior art (see p.2). However, the relevance of sambiasin-1 (SEQ ID NO:1) to Alzheimer's disease or Notch cleavage at the time of invention appears to be unknown since no further characterization of sambiasin-1 (SEQ ID NO:1) has been provided except its potential interacting partners.

The instant claims 21-28 and 49 are drawn to a method for screening for a molecule that modulates the function, activity, composition or formation of a protein complex having a first protein sambiasin-1 (SEQ ID NO:1) and a second protein, selected from presenilin-1 (SEQ ID NO:2) and nicastrin (SEQ ID NO:3) or their functionally active fragments/derivatives/homologs/variants, by exposing the complex to a test compound that is able to bind to the complex. In the absence of knowledge of the biological significance or relevance to a particular pathological condition of this specific protein-protein interaction of sambiasin-1 and presenilin-1 or nicastrin there is no immediately obvious patentable use for a method of screening for a molecule that modulates such complexes. The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant sambiasin-1 and presenilin-1/nicastrin protein complexes are associated with any diseases or disorder, and does not provide a nexus between sambiasin-1 and presenilin-1/nicastrin complexes and Alzheimer's disease or APP processing or Notch cleavage as asserted in the specification. Applicant fails to provide sufficient guidance as to identify or confirm a "real world" context of use; clearly further research would be required to identify a disease in which the protein complex is involved and a relationship between sambiasin-1 and presenilin-1/nicastrin in a disease. Thus, further research is required to identify a

disease for which it could be used, or a disease for which its presence would be diagnostic. Furthermore, identification of molecules that affects the function/activity/composition/formation of the claimed complex is useful only in research to determine the function of the protein complex itself: there is no "specific benefit in currently available form" to be derived from such studies since the relevance of the claimed complex to a disease is unknown. Applicant thus does not identify or confirm a "real world" context of use; clearly further research would be required to identify a disease or function associated with this protein complex.

There is little doubt that, after complete characterization, the protein complex comprising sambiasin-1, presenilin-1 and nicastrin may be found to have a specific and substantial credible utility. However, this further characterization is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful

conclusion." A patent is therefore not a license to experiment. See also the Revised Interim Utility Guidelines available at www.uspto.gov.

The claimed invention also lacks a well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The instant claims 21-28 and 49 are drawn to a method of screening for a molecule that modules the function, activity, composition or formation of a protein complex having a first protein sambiasin-1 or its functional fragments/derivatives/homologs/variants, and a second protein presenilin-1/nicastrin or its functional fragments/derivatives/homologs/variants. Although Applicant states that the present invention relates to the field of neurodegenerative diseases, specifically Alzheimer's disease (AD) or embryo development or developmental disorders caused by a defect of the Notch signaling pathway, it also states that "Despite the large body of information already available from the prior art concerning presenilin proteins, up to now the picture of presenilin-interactor proteins remains elusive." (page 2, [003]). Since the significance of a complex of sambiasin-1, presenilin-1 and nicastrin or their functional fragments/derivatives at present is not fully established and the relationship of sambiasin-1 with presenilin-1 is not understood, it is also unclear that how the proteins in the claimed protein complexes are related to the process of neurodegeneration/development or the etiology and pathogenesis of neurodegenerative diseases or developmental disorders caused by a defect of the Notch signaling pathway. Applicant states that "a method of screening for a drug for treatment or

prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer and developmental disorders caused by defects in the Notch pathway. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 to 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer and developmental disorders caused by defects in the Notch pathway" (see page 24 of the specification). However, in the absence of knowledge of the biological significance or relevance to a particular pathological condition of this specific protein-protein interaction of sambiasin-1, presenilin-1 and nicastrin or their functional fragments/derivatives, there is no immediately obvious patentable use for such complexes. The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant sambiasin-1, presenilin-1 and nicastrin complexes are associated with any diseases or disorder, and does not provide a nexus between sambiasin-1, presenilin-1 and nicastrin in Alzheimer's disease or developmental disorders caused by a defect of the Notch signaling pathway as asserted in the specification. To screen for molecules that modules the protein complex comprising first protein sambiasin-1 and a second protein presenilin-1/nicastrin and identifying molecules for modulating their interaction are thus not a "real world" use because it would eventually relate to a complex of proteins for which no biological significance is established. In addition, to identify a molecule that modulates the protein complex comprising first protein sambiasin-1 or its fragments/derivatives/homologs/variants with a second protein selected from presenilin-

1/nicastrin its fragments/derivatives/homologs/variants for the treatment of a disease as in claim 28 is not a "real world" use because it would eventually relate to a complex of proteins for which no biological significance is established and no relevance to a specific disease. Potential discovery of a compound that modulates the interaction of proteins in the disclosed complexes would not lead to prevention or treatment of a condition or disease as implied by the specification because without knowing functional significance of the interaction between sambiasin-1 and presenilin-1/nicastrin or their fragments/derivatives/homologs/variants and the relevance to the disease one would not expect that modulation of such interaction would have a considerable impact on the treatment of a disease. Since the instant specification does not disclose a substantial "real world" use for the protein-protein complex of its functionally active fragments/derivatives/homologs/variants, then the claimed invention of screening a molecule that modulates the complex is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-28 and 49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted

utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 21-28 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, were it enabling for a protein complex comprising sambiasin-1 (SEQ ID NO:1) and presenilin-1 (SEQ ID NO:2) by immunoprecipitation using anti-presenilin and identifying a molecule/an antibody that binds to the protein complex or potential binding partners, does not reasonably provide enablement for identifying a molecule that modulates an protein complex having a first protein that is sambiasin-1or its functional fragments/derivatives/homologs/variants and a second protein that is selected from presenilin-1 and nicastrin or their functional fragments/derivatives/homologs/variants as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Claims 21-27 and 49 are directed to a method of screening for a molecule that modulates a protein complex comprising a first protein sambiasin-1 or its functional fragments/derivatives/homologs/variants and a second protein selected from presenilin-1 and nicastrin or their functional fragments/derivatives/homologs/variants. Applicant reported a direct interaction between sambiasin-1 and presenilin-1, which is identified by immunoprecipitation of brain homogenates using an anti-presenilin antibody to isolate the protein complex and sequencing the protein complex by mass spec. Applicant is enabled for isolating the protein complex comprising sambiasin-1 and presenilin-1, as originally filed. Based on the specification and prior art, Applicant could be predictably enabled for isolating a protein complex comprising sambiasin-1, presenilin-1 and nicastrin. Applicant is also predictably enabled for identifying a molecule/antibody/protease that binds to the protein complex to affect the function/activity/composition/formation of the complex. However, the instant specification, as filed, provides insufficient guidance as to enable one skilled in the art how to make/use the full scope of the claimed method since Applicant fails to provide

guidance as to what specific conserved structures/characteristics of the functionally active fragments/derivatives/homologs/variants of sambiasin-1, presenilin-1 or nicastrin are required to maintain the interaction between two homologue proteins in an isolated protein complex. It has been shown that a single amino acid change can alter the function of a protein. For example, a substitution of lysine residue by glutamic acid at position 118 of acidic fibroblast growth factor results in a substantial loss of its biological activity including the binding ability to heparin and its receptor (Burgess et al. J of Cell Bio. 111:2129-2138, 1990). A change of an amino acid sequence would change a protein conformation, which consequently changes the binding ability of the peptide to its binding partner or receptors. In addition to a core determinant sequence, the protein-protein interaction also relies on the flanking or noncontiguous residues (see p. 445 the second column, first paragraph, Pawson et al. 2003, Science 300:445-452). The optimal binding motif for a domain is not necessarily suitable for physiological or in vivo interaction. The predictive data always need to be validated by actual analyses in cells (see p. 445, the third column, second paragraph, Pawson et al. 2003, Science 300:445-452). Applicant fails to provide guidance as to what functional regions of the claimed fragments/derivatives/homologs/variants of sambiasin-1, presenilin-1 or nicastrin are. Applicant fails to disclose the common conserved functional structures/characteristics of these fragments/derivatives/homologues/variants that are required for forming a protein complex. A skilled artisan cannot predict the function/activity of these claimed fragments/derivatives/homologues/variants. Since the required conserved structures/characteristics of the fragments/derivatives/homologs/variants of sambiasin-

1, presenilin-1 or nicastrin are not unknown, it is unpredictable whether these claimed fragments/derivatives/homologs/variants of sambiasin-1, presenilin-1 or nicastrin could maintain the binding ability to each other and form a complex, indicating that undue experimentation is required to practice the claimed invention. Since it is unpredictable whether the claimed fragments/derivatives/homologs/variants of sambiasin-1, presenilin-1 or nicastrin can maintain the binding ability to each other and form a complex, it is also unpredictable what specific results would be obtained in a screening method of using these claimed complexes.

Claim 28 is directed to a method of screening for a drug for treatment or prevention of a disease selecting from a neurodegenerative disease and a developmental disorder caused by a defect in the Notch signaling. Presenilin-1 and nicastrin have been shown that they could be potentially involved in the process of neurodegeneration and embryo development (see p.11 of the specification). However, the art does not recognize any involvement of any particular protein complex or any interaction between sambiasin-1 and presenilin-1/nicastrin in Alzheimer's pathology or embryo development or developmental disorders caused by a defect of the Notch signaling pathway(see p. 29, abstract, Pastorino et al. Eur. J. Pharmacol. 2006. 545: 29-38). The molecules involved in pathogenesis of Alzheimer's disease and APP processing include β-secretase (BACE1), γ-secretase (presenilin 1/2, Nicastrin, Aph1 and Pen2) and phosphorylation of APP (PKC, CamKII, GSK3, cdk5) and cholesterol related molecules (LRP). The Notch signaling pathway has been shown to be involved in neurogenesis, cancer, development of lymphocytes and CADASIL (Cerebral

Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) (p. 324, section 5. Notch and disease, Hansson et al. Semin Cancer Biol. 2004. 14: 320-328). Sambiasin-1 has not been demonstrated to be involved in the Notch signaling pathway and APP processing (see p. 568; p. 574, last paragraph to p. 575, 1st paragraph, Selkoe et al. Annu. Rev. Neurosci. 2003. 26: 565-97). Neither the art nor the specification has established the involvement of the claimed complex is related to any neurodegenerative disease or developmental disorders caused by a defect of the Notch pathway. Thus, it is unpredictable whether a molecule that is identified as a modulator to affect a specific function/activity/composition/formation of the protein complex comprising sambiasin-1 and presenilin-1/nicastrin would be useful to treat or prevent any neurodegenerative disease or developmental disorder caused by a defect of the Notch signaling pathway since the role of the protein complex is unknown in any of neurodegenerative diseases or developmental disorders related to a defect of the Notch signaling pathway and the cause of the diseases is not known. Thus, Applicant has not provided sufficient guidance as to enable one of skill in the art to practice the claimed invention.

Therefore, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to a method of screening for a molecule that modulates a protein complex comprising a first protein sambiasin-1 or its

functional fragments/derivatives/homologs/variants and a second protein selected from presenilin-1 and nicastrin or their functional fragments/derivatives/homologs/variants.

Claims 21-28 and 49 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Claims 21-28 and 49 are directed to a method of screening for a molecule that modulates a protein complex comprising a first protein sambiasin-1 or its functional fragments/derivatives/homologs/variants and a second protein selected from presenilin-1 and nicastrin or their functional fragments/derivatives/homologs/variants. The claims do not require that the protein complex possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims encompass a genus of protein complexes. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to

understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of a protein complex of sambiasin-1 and presenilin-1 molecules that can be used in the claimed method. However, the claims are drawn not only to the full-length proteins but also to their functional fragments/derivatives/homologs/variants. Applicant is not in possession of all protein complexes that could be used in the claimed method. The specification only describes sambiasin-1/2, presenilin-1/2 and nicastrin proteins and fails to teach or describe any other protein. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of sambiasin-1, presenilin-1 and nicastrin. While a generic sequence is provided, there is merely a set of common properties: there is no description of the conserved regions which are critical to the function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the polypeptides with limited homology in the genus from other proteins are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides or protein complexes encompassed: there is no guidance in the art as to what the defining characteristics of an isolated protein complex comprising a first protein of sambiasin-1 and a second protein selecting from presenilin-1 and nicastrin or their functional fragments/derivatives/homologs/variants might be. Since the common characteristics/features of the sambiasin-1, presenilin-1 and nicastrin and their

functional fragments/derivatives/homologs/variants in an isolated protein complex are unknown, a skilled artisan cannot contemplate the functional correlations of the genus with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, a method of screening for a molecule that modulates a protein complex comprising a first protein sambiasin-1 or its functional fragments/derivatives/homologs/variants and a second protein selected from presenilin-1 and nicastrin or their functional fragments/derivatives/homologs/variants have not met

the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-28 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a detecting step to determine/detect whether the candidate molecule is bound to the complex in claims 21 and 49. The omitted steps are: a detecting step to determine and evaluate the activity/function of the protein complex in claim 22. The rest of claims are dependent claims.

Claims 22-28 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-28 and 49 are indefinite because Applicant recites "function", "activity" and "change" in claims 22, 24, 27, and recites "physiological substrate" in claim 25. Although Applicant describes activities as enzymatic activity or inhibiting/stabilizing the

protein or subcellular location on p.12, this description is not definite: there is no limitation on what would or would not be considered an "activity" and thus be within the scope of the claims. Applicant also fails to define what specific function of the protein complex is and how it can be changed and can be considered as effective. Applicant fails to define/specify what is/is not included within the limitations of the claims. The disclosure also fails to set for the metes and bounds of what is encompassed within the definition of "function" and "change". Thus the artisan would not know what responses Applicant intended to measure.

Claims 22-28 are indefinite because claim 22 depend from claim 1 and Applicant recites functionally active fragments/derivatives/homologs/variants in claim 1 and claim 27. Although Applicant describes "derivatives/variants/homologs on p. 15 of the specification, it is not clear what is encompassed in the definition of "functionally active fragments/derivatives/homologs/variants". The disclosure also fails to set for the metes and bounds of what is encompassed within the definition of "functionally active fragments/derivatives/homologs/variants". These descriptions are indefinite because there is no limitation on what would or would not be included in a "functionally active fragments/derivatives/homologs/variants" and thus be within the scope of the claims. In addition, claim 28 is indefinite because the recitation of developmental disorders caused by a defect in the Notch pathway. The disclosure fails to set for the metes and bounds of what is encompassed within the definition of "developmental disorders caused by a defect in the Notch pathway" because it is unknown what specific defect of the Notch pathway would be associated with what specific developmental disorder. Thus, a skilled

artisan does not known how to evaluate the effect of the test molecule/compound and determine whether the test molecule/compound could be used to treat a developmental disorder.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 49 is rejected under 35 U.S.C. 102(e) as being anticipated by U. S. Patent No. 6913919 (issued Jul 5, 2005, priority date Jun 17, 1998).

U. S. Patent No. 6913919 teaches SEQ ID NO:303, which has 100% identity to the instant SEQ ID NO:1 (Sambiasin-1). '919 teaches a method of screening for a compound that bind to SEQ ID NO: 303 (instant SEQ ID NO:1), which meets the limitation as in claim 49 (see col. 509, Example 146). '919 also teaches a method of making/preparing an antibody against SEQ ID NO:303 (instant SEQ ID NO:1) (see col. 507-508, Examples 144-145). The method of making and preparing antibodies against SEQ ID NO:303 also involves identifying whether the antibodies bind to the polypeptide, which meets the limitation as in claim 49. Therefore, claim 49 is anticipated by U. S. Patent No. 6913919.

The sequence search results disclose as follows:

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US-09-991-181-303
; Sequence 303, Application US/09991181
; Patent No. 6913919
; GENERAL INFORMATION:
;  APPLICANT: Ashkenazi,Avi J.
;  APPLICANT:  Baker,Kevin P.
;  APPLICANT:  Botstein,David
;  APPLICANT:  Desnoyers,Luc
;  APPLICANT:  Eaton,Dan L.
;  APPLICANT:  Ferrara,Napoleone
;  APPLICANT:  Fong,Sherman
;  APPLICANT:  Gerber,Hanspeter
;  APPLICANT:  Gerritsen,Mary E.
;  APPLICANT:  Goddard,Audrey
;  APPLICANT:  Godowski,Paul J.
;  APPLICANT:  Grimaldi,J.Christopher
;  APPLICANT:  Gurney,Austin L.
;  APPLICANT:  Kljavin,Ivar J.
;  APPLICANT:  Napier,Mary A.
;  APPLICANT:  Pan,James
;  APPLICANT:  Paoni,Nicholas F.
;  APPLICANT:  Roy, Margaret Ann
;  APPLICANT:  Stewart, Timothy A.
;  APPLICANT:  Tumas, Daniel
;  APPLICANT:  Watanabe, Colin K.
;  APPLICANT:  Williams, P. Mickey
;  APPLICANT:  Wood, William I.
;  APPLICANT:  Zhang, Zemin
;  TITLE OF INVENTION: Secreted and Transmembrane Polypeptides and Nucleic
;  TITLE OF INVENTION:  Acids Encoding the Same
;  FILE REFERENCE: P2730P1C53
;  CURRENT APPLICATION NUMBER: US/09/991,181
;  CURRENT FILING DATE:  2001-11-16
;  PRIOR APPLICATION NUMBER: 60/049787
;  PRIOR FILING DATE: 1997-06-16

  Query Match             100.0%;  Score 1256;  DB 2;  Length 247;
  Best Local Similarity   100.0%;  Pred. No. 8.4e-128;
  Matches  247;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIILVAGAFFWLVSLLLASVVWFILVHVT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIILVAGAFFWLVSLLLASVVWFILVHVT 60

Qy         61 DRSDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 DRSDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYV 120

Qy        121 SGLSFGIISGVFSVINILADALGPGVVGIHGDSPYYFLTSAFLTAAIILLHTFWGVVFFD 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

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Db        121 SGLSFGIISGVFSVINILADALGPGVVGIHGDSPYYFLTSAFLTAAIILLHTFWGVVFFD 180

Qy        181 ACERRRYWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 ACERRRYWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQ 240

Qy        241 RSLLCKD 247
              |||||||
Db        241 RSLLCKD 247
```

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 6:00 PM. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
December 12, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER